IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENETIC TECHNOLOGIES LIMITED,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 12-394 (LPS)
	)	
BRISTOL-MYERS SQUIBB COMPANY,	)	
	)	
Defendant.	)	

OPENING BRIEF IN SUPPORT OF DEFENDANT BRISTOL-MYERS SQUIBB'S MOTION TO DISMISS UNDER FEDERAL RULE OF CIVIL PROCEDURE 12(b)(6) FOR FAILURE TO STATE A CLAIM

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INTRODUCTION

Plaintiff Genetic Technologies Ltd. ("GTG") asserts U.S. Patent No. 5,612,179 ("'179 Patent") and U.S. Patent No. 5,851,762 ("'762 Patent") against defendant Bristol-Myers Squibb Co. ("BMS"). The patents in suit concern technology related to deoxyribonucleic acid ("DNA"). Second Am. Compl. ("SAC") ¶ 7 (D.I. 31). In particular, as further explained below, GTG alleges that the named inventor of both patents, Malcolm Simons, "discovered" that sequences in "non-coding" regions of DNA (that is, sequences in DNA that do not contain blueprints for synthesizing proteins) are sometimes linked or correlated (inherited together) with sequences in "coding" regions of DNA (that is, sequences that do contain such blueprints). *Id*. ¶ 17. As a result, genetic variations (sometimes referred to by GTG as "alleles" or "polymorphisms") in the coding regions can allegedly be detected indirectly, by analyzing noncoding-region sequences. *Id*. In GTG's words, the patents in suit "reveal the discovery that non-coding region polymorphisms can be mapped and used as surrogate markers for coding region polymorphisms." *Id*. ¶ 22.

This "discovery," however, is not patentable subject matter under 35 U.S.C. § 101. Rather, it is a discovery of a law of nature. GTG has not added any steps to its patent claims that would transform this law of nature into a patentable invention. As GTG states, the tools a person of skill in the art would have used to observe such correlations between variations in noncoding- and coding-region sequences of DNA were well known in the art at the time of Dr. Simons's alleged discovery. *See, e.g.*, SAC ¶ 25. Accordingly, GTG's complaint against BMS should be dismissed.[1]

[1] The instant motion focuses on the narrow and dispositive issue of whether the patents cover patentable subject matter. To the extent this motion is not granted, BMS intends to raise numerous additional defenses including non-infringement and additional invalidity defenses.

NATURE AND STAGE OF THE PROCEEDINGS

GTG, a non-practicing entity, initiated the present litigation on May 25, 2011, when it filed suit against BMS and nine unrelated entities in the U.S. District Court for the District of Colorado, alleging direct and indirect infringement of the '179 patent. Complaint, *Genetic Techs. Ltd. v. Agilent Techs., Inc.*, Civil Action No. 11-cv-01389-WJM-KLM (D. Colo. May 25, 2011), E.C.F. No. 1. GTG asserted that BMS infringed the '179 patent by undertaking genetic research associated with its drug products Coumadin® and Plavix®, among others. *Id.* ¶¶ 35-52. The allegedly infringing activity of the other nine defendants varied widely and ranged from offering seed sampling services for the plant breeding industry (Defendant Eurofins), *id.* ¶¶ 53-64, to offering a genotyping service to cattle farmers (Defendant Merial), *id.* ¶¶ 84-89.

In September 2011, GTG filed a First Amended Complaint. D.I. 2. In March 2012, the Court granted BMS's motion to sever the claims pending between GTG and BMS from unrelated claims between GTG and the other defendants. Order, *Genetic Techs. Ltd. v. Agilent Techs., Inc.*, Civil Action No. 11-cv-01389-WJM-KLM (D. Colo. March 28, 2012), E.C.F. No. 314. The Court also granted BMS's request to transfer the claims against it to this District. *Id.* The case against BMS, along with GTG's claims against defendants Merial and Pfizer, were assigned to Judge Robinson and coordinated for pretrial discovery. GTG then moved to combine the actions that had been severed and transferred out of Colorado back into a multi-district proceeding. D.I. 11; D.I. 17. After the MDL panel denied GTG's motion in 2012, Judge Robinson stayed the cases on the parties' joint request pending reexamination proceeding of the '179 Patent initiated by Merial in the U.S. Patent and Trademark Office. D.I. 19; D.I. 23; D.I. 24; D.I. 25. In November 2013, Judge Robinson lifted the stay of the BMS, Pfizer, and Merial cases and granted GTG leave to amend its complaint a second time. D.I. 28. Subsequently, the BMS, Pfizer, and Merial cases were reassigned to Judge Stark and coordinated with the two cases

involving the '179 Patent filed by GTG against Natera and Histogenetics in 2012. D.I. 30. GTG filed its Second Amended Complaint ("SAC") against BMS in December 2013, asserting for the first time that BMS infringed a second patent, the '762 Patent. *See* SAC. GTG acknowledged that it has asserted its patents against and/or extracted royalties from some 40 different entities. *Id.* ¶¶ 43-46.

SUMMARY OF THE ARGUMENT

1. The claims of both patents are directed to naturally occurring correlations or linkages between different regions of DNA, which are not patentable subject matter under 35 U.S.C. § 101. *See Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 132 S. Ct. 1289, 1293 (2012).

2. The additional limitations of the claims, such as the "amplification" steps, "add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field," and are therefore not sufficient to save such claims that focus upon a law of nature. *Id*. at 1299; *see also Ultramercial, Inc. v. Hulu, LLC*, 722 F.3d 1335, 1347-48 (Fed. Cir. 2013).

FACTUAL BACKGROUND

GTG alleges that the named inventor of both patents in suit, Malcolm Simons, "discovered" that sequences in "noncoding" regions of DNA are sometimes linked or correlated with sequences in "coding" regions of DNA, such that certain genetic variations in coding regions can be detected indirectly, by analyzing noncoding region sequences. SAC ¶ 17[2]; *see*

[2] Although for purposes of this motion the Court must accept as true GTG's factual allegations in the SAC, including those describing the technology, BMS's citation to such allegations for purposes of this motion is without prejudice to its right to dispute those characterizations at a later time, including during claim construction.

also '179 Patent, 4:6-11 (A4)[3]; '762 Patent, 7:16-19 (A38); *see generally* SAC ¶¶ 11-13, 16-17 (describing how correlations between coding and noncoding sequences arise from basic principles of reproductive biology). As GTG alleged in its SAC, the patents in suit "reveal the discovery that non-coding region polymorphisms can be mapped and used as surrogate markers for coding region polymorphisms." *Id*. ¶ 22. In general, GTG asserts that the '179 Patent is directed to "amplifying" sequences of DNA and "analyzing" them, with the aim of using known correlated variations in noncoding and coding regions to detect a genetic sequence. SAC ¶¶ 17-19, 39 (citing claim 1 of the '179 Patent). Similarly, GTG asserts that the '762 Patent generally is directed to "genomic mapping," or determining the location of a gene associated with a trait (*e.g.*, a particular disease) by examining patterns of noncoding-region variations. *Id*. ¶¶ 16, 42 (citing claim 1 of the '762 Patent).[4] Both patents are based on implementing Dr. Simons's sole alleged discovery.

Scientific Background. An organism's "genome" is its complete set of genetic material. In humans, genetic information is encoded in deoxyribonucleic acid ("DNA") based on the order of the individual nucleotides in the DNA. SAC ¶ 7. A "gene" is a region of the genome that contains all the information needed to assemble a particular protein. '179 Patent, 6:16-23 (A5);

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[3] The patents in suit, along with selections from their prosecution histories, may be found in the accompanying Appendix to BMS's Opening Brief in Support, cited as A__. The entire prosecution histories have not been provided due to their excessive length (over 2,500 pages), but BMS can provide the entire file histories to the Court upon request.

[4] The SAC specifically discusses only claim 1 of the '179 patent and claim 1 of the '762 patent. To the extent GTG argues in response to this motion that it intends to assert additional patent claims against BMS, GTG has not met its pleadings obligations under Rule 8 of the Federal Rules of Civil Procedure, notwithstanding that the SAC is the *third* pleading GTG has filed against BMS. *See Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) ("[T]he pleading standard Rule 8 announces does not require 'detailed factual allegations,' but it demands more than an unadorned, the-defendant-unlawfully-harmed-me accusation." (quoting *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007)).

'762 Patent, 9:18-24 (A39). As discussed above, GTG claims that the asserted patents are directed to a particular relationship between naturally occurring genetic materials: "coding sequences" and "noncoding sequences." A "coding sequence," also known as a "coding region" or an "exon," is a segment of an organism's genome that contains encoded instructions for putting together amino acids to form a particular protein. '179 Patent, 5:40-50, 60:4-5 (A5, A32); '762 Patent, 8:50-53 (A37); SAC ¶ 13. A "noncoding" sequence or region, or "intron," by contrast, is a portion of the genome that does not contain encoded instructions for putting together amino acids. '179 Patent, 5:40-50 (A5); '762 Patent, 8:49-56 (A38). A typical gene consists of interspersed coding and noncoding sequences, while the portions of the genome between genes consist entirely of noncoding sequences. '179 Patent, 5:40-50 (A5); '762 Patent, 8:49-56 (A38); SAC ¶ 13. The existence of coding and noncoding sequences was well known before GTG's patent. *See, e.g.*, '179 Patent, 3:39-47, 5:40-50 (A4, A5); '762 Patent, 6:23-32, 8:49-56 (A37, A38); SAC ¶ 15.

A "polymorphism" is a variation between different individuals' genetic codes at a particular site in the genome. SAC ¶ 9. Polymorphisms can occur at coding and noncoding sites. '179 Patent, 5:3-9 (A5); '762 Patent, 11:46-56 (A40).[5] When a polymorphism occurs at a site located within a coding region, each version of that polymorphic site is known as an "allele." '179 Patent, 5:18-20 (A5); '762 Patent, 8:25-29 (A38); SAC ¶ 9.

Prior to the '179 Patent, it was common for scientists studying DNA to "amplify" the portion of interest by making additional copies. '179 Patent, 2:45-60, 3:5-12, 3:39-45, 5:55-6:3, 12:53-65 (A3, A4, A5-A6, A8); '762 Patent, 8:58-62 (A38). One common method for

[5] *See also* Am. in Resp. to Final Office Action of March 21, 1994, at 13 (June 20, 1994) ('762 Patent) (A165) ("[T]he [prior] art clearly holds that all genetic loci include non-coding sequence polymorphisms.").

amplifying DNA was "polymerase chain reaction," or "PCR." '179 Patent, 2:45-60, 3:5-12 (A3, A4); '762 Patent, 22:23-41 (A45). In PCR, a "primer pair" (a pair of short, human-made strands of DNA, each matching a specific short sequence along the genome) is used in conjunction with an enzyme known as a "polymerase" to create copies of the longer stretch of genome flanked by the two short sequences. '179 Patent, 2:45-60, 3:5-12, 5:66-6:3, 6:10-13 (A3, A4, A5, A6); '762 Patent, 9:1-5 (A37); SAC ¶¶ 23-24. As acknowledged in the patents in suit, PCR was disclosed in 1985, well before the applications leading to GTG's patents were filed. '179 Patent, 2:46-60 (A3); '762 Patent, 22:27-30 (A45). Moreover, GTG states that PCR was known in the art at the time of Dr. Simons's alleged discovery. SAC ¶ 25.

ARGUMENT

I. Dismissal for Failure To State a Claim Is Appropriate When a Patent Claims a Law of Nature.

A. Standard for a Motion To Dismiss for Failure To State a Claim

Although the Court must accept the factual allegations in the SAC as true, "when the allegations in a complaint, however true, could not raise a claim of entitlement to relief, 'this basic deficiency should … be exposed at the point of minimum expenditure of time and money by the parties and the court.'" *Bell Atl. Corp. v Twombly*, 550 U.S. 544, 558 (2007) (quoting 5 Charles Alan Wright *et al.*, *Federal Practice & Procedure: Civil* § 1216, at 233-34). Dismissal under Rule 12(b)(6) based on the subject-matter ineligibility of the patents in suit is appropriate when "the only plausible reading of the patent [shows] that there is clear and convincing evidence of ineligibility." *Ultramercial*, 722 F.3d at 1339 (emphasis removed). Accordingly, this Court has recently granted defendants' Rule 12 motions on grounds of subject-matter ineligibility. *See UbiComm, LLC v. Zappos IP, Inc.*, C.A. No. 13-1029-RGA, 2013 WL 6019203

(D. Del. Nov. 13, 2013) (Rule 12(b)(6) motion); *BuySAFE, Inc. v. Google Inc.*, C.A. No. 11-1282-LPS, 2013 WL 3972261 (D. Del. July 29, 2013) (Rule 12(c) motion).

In reviewing this Motion, the Court should disregard those "allegations" in GTG's complaint that merely state legal conclusions. *See Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009); *Great W. Mining & Mineral Co. v. Fox Rothschild LLP*, 615 F.3d 159, 177 (3d Cir. 2010). This includes GTG's "allegations" that "[t]he '179 Patent and '762 Patent claim patentable subject matter under 35 U.S.C. § 101," and that "the correlation of non-coding DNA polymorphisms with coding region alleles" is not a law of nature for purposes of § 101. SAC ¶¶ 21, 35. "[T]he tenet that a court must accept as true all of the allegations contained in a complaint is inapplicable" to such "legal conclusions." *Iqbal*, 556 U.S. at 678.

It is, however, appropriate for the Court to consider the '179 and '762 Patents, both of which are attached to the complaint. Fed. R. Civ. P. 10(c). The Court may also take judicial notice of the prosecution histories of the patents in the Patent and Trademark Office, which are "public records." *See Lum v. Bank of Am.*, 361 F.3d 217, 222 n.3 (3d Cir. 2004); *Hockerson-Halberstadt, Inc. v. Avia Group Int'l, Inc.*, 222 F.3d 951, 957 (Fed. Cir. 2000); *Classen Immunotherapies, Inc. v. Shionogi, Inc.*, Civil Case No. RWT-13-921, 2014 WL 323941, at *1 n.1, *8 n.10 (D. Md. Jan. 29, 2014); *RB Rubber Prods., Inc. v. ECORE Int'l, Inc.*, Civ. No. 3:11-cv-319-AC, 2012 WL 860416, at *4-5 (D. Or. Mar. 13, 2012) (nonprecedential); *Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.*, No. C-92-20643 RMW, 1994 WL 270714, at *2 (N.D. Cal. Apr. 19, 1994) (nonprecedential), *aff'd without opinion*, 104 F.3d 376 (Fed. Cir. 1996).

B. Standard for Subject-Matter Ineligibility under § 101

The Supreme Court has recognized three categories of subject matter that are ineligible for patenting under 35 U.S.C. § 101: "[L]aws of nature, natural phenomena, and abstract ideas."

See Mayo, 132 S. Ct. at 1293 (quotation marks omitted). Such ineligible subject matter cannot be claimed even if limited "to one field of use" or "to a particular technological environment." *Id*. at 1297, 1301 (quotation marks omitted). Nor will the addition of other limitations save a claim that focuses upon a law of nature unless "the claims do *significantly* more than simply describe these natural relations." *Id.* at 1297 (emphasis added). The Supreme Court has explained that "a process that focuses upon the use of a natural law [must] also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Id*. at 1294. Claim limitations that "add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field" are insufficient. *Id*. at 1299; *SmartGene, Inc. v. Advanced Biological Labs., SA*, No. 2013-1186, 2014 WL 259824, at *5 (Fed. Cir. Jan. 24, 2014) (nonprecedential).

Further, the Federal Circuit has held that a method claim lacks an "'inventive concept'" if "implementing the [natural law] in the context of the claimed invention *inherently requires the recited steps*"; the steps are "*routine and conventional aspect[s]*" of the natural law; or the steps recite "only *abstract mental processes*." *See Ultramercial*, 722 F.3d at 1347-48 (emphasis added); *Ass'n for Molecular Pathology v. USPTO* (*AMP I*), 689 F.3d 1303, 1334 (Fed. Cir. 2012), *aff'd in part and rev'd in part on other grounds sub nom. Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* (*AMP II*), 133 S. Ct. 2107 (2013).

The courts have repeatedly relied on these principles to invalidate claims that do no more than append conventional, inherent, or mental steps to laws and phenomena of nature. For example, in *Mayo*, the Supreme Court invalidated claims drawn to a method of administering a drug and observing concentrations of the drug's metabolites in the patient's bloodstream,

wherein the metabolite levels indicated whether the dose was proper. *See Mayo*, 132 S. Ct. at 1295.

In addition, in *AMP I*, the Federal Circuit invalidated claims to "analyzing" genetic material taken from a subject and "comparing" material from a tumor sample with material from a nontumor sample. *See* 689 F.3d at 1334-35.[6]

And in *PerkinElmer, Inc. v. Intema Ltd.*, the Federal Circuit invalidated claims that recited directions for collecting data on the health of a pregnant woman and her fetus and instructed the practitioner to "determin[e] the risk of Down's syndrome by comparing" those data with "observed relative frequency distributions of marker levels in Down's syndrome pregnancies and in unaffected pregnancies." 496 F. App'x 65, 66-68 (Fed. Cir. 2012) (nonprecedential). The court observed that the claims recited both a law of nature ("the relationship between screening marker levels and the risk of fetal Down's syndrome") and an abstract idea ("the mental process of comparing data to determine a risk level"), and that the remaining limitations of the claims consisted entirely of "'well-understood, routine, conventional activity previously engaged in by scientists who work in the field.'" *Id.* at 70-71 (quoting *Mayo*, 132 S. Ct. at 1298).

II. The '179 and '762 Patents Claim Ineligible Subject Matter Because They Claim a Law of Nature.

A. The '179 and '762 Patents Claim a Law of Nature Relating to Correlating Coding and Noncoding Regions of DNA.

The '179 and '762 Patents both "focus[] upon" correlating coding and noncoding regions of DNA. *See Mayo*, 132 S. Ct. at 1294. This is nothing more than a law of nature. GTG may

[6] The Supreme Court subsequently reversed the Federal Circuit's holding on other claims of the patents but did not review its holdings regarding the method claims. *See AMP II*, 133 S. Ct. at 2113 & n.2, 2119.

assert that they have added additional steps, such as amplifying and analyzing DNA, s*ee, e.g.*, SAC ¶ 26, but this does not overcome the simple fact that they did not invent anything new beyond the alleged discovery of an existing law of nature.

The specification of the '179 Patent states that "[t]he present invention is based on the finding that [naturally occurring] intron sequences contain genetic variations that are characteristic of adjacent and remote alleles on the same chromosome." '179 Patent, 4:6-8 (A4); SAC ¶¶ 17, 22.[7] The specification of the '762 Patent similarly states that "[t]he present invention is based on the finding that non-coding region sequences, particularly intron sequences, contain genetic variations that are characteristic of alleles of adjacent and remote, linked genetic loci on the chromosome." '762 Patent, 7:16-19 (A38).

However, the alleged "finding," which underlies both patents, is a paradigmatic "law of nature." *See also* SAC ¶¶ 16, 22 (acknowledging that "the inventions of the '179 Patent and '762 Patent are based on," and "reveal," Dr. Simons's "discovery" regarding coding- and noncoding-region polymorphisms). Although particular linked sets of coding and noncoding regions may come and go in a population's genome, the fact that such correlated sets exist is a consequence of basic principles of reproductive biology, and has itself existed for eons. *See* SAC ¶¶ 11-13, 16-17 (describing how such correlations arise from basic principles of reproductive biology); *see also AMP II*, 133 S. Ct. at 2111, 2116 (holding "that a naturally occurring DNA segment is a product of nature [even when] it has been isolated" because "[t]he location and order of the nucleotides existed in nature before [the patentee] found them"); *Mayo*,

[7] This statement is echoed in the prosecution history, which emphasizes that "[t]he basis of Applicant's invention is that variations (polymorphisms) in the non-coding regions are also indicative of the coding region allele." Am. in Resp. to Office Action of March 25, 1993, at 19 (Sept. 24, 1993) ('179 Patent) (A93).

132 S. Ct. at 1296-97 (holding that the claims in suit "set forth laws of nature" because the "relationship[]" they embodied, "between concentrations of … metabolites … and the likelihood that a dosage … will prove ineffective or cause harm," was "a consequence of the ways in which [drugs] are metabolized by the body—entirely natural processes").[8]

GTG's assertion that the exon-intron relationship at the heart of its claims is not "ineluctable," "generally applicable," or "present in all species or … individuals of a particular species," and "may not have existed in the past [or] exist in the future," is irrelevant. SAC ¶ 21.[9] The Supreme Court "ha[s] not distinguished among different laws of nature according to whether or not the principles they embody are … narrow." *Mayo*, 132 S. Ct. at 1303. Even a single, specific naturally occurring correlation between two observable quantities is a patent-ineligible "law of nature." *See id.* at 1295 (holding that the correlation between the dosage of a certain drug and the concentration of its metabolites in the bloodstream is a law of nature). GTG does not argue that the patents' claims are so limited, however, but rather appears to assert that the

[8] In fact, the '179 and '762 Patents more clearly set forth a law of nature than the patents at issue in *Mayo*. In *Mayo*, it took a "human action (the administration of a ... drug) to trigger a manifestation of th[e] relation in a particular person." 132 S. Ct. at 1297. By contrast, no "human action" is required to "trigger a manifestation" of the correlation between linked coding and noncoding sequences, which exists naturally in the genomes of humans and other species, observed or unobserved.

[9] In any event, GTG's current characterization of this phenomenon as something other than "generally applicable" is diametrically opposed to the patentee's characterization of the phenomenon during prosecution. In response to an examiner rejection of the application that led to the '179 Patent, the patentee submitted a declaration by a plant geneticist stating that "the basis for [the named inventor's] analysis system applies to all eukaryotic genomes," and that "the phenomenon that non-coding region sequences contain informative polymorphisms that can be used to identify associated coding region alleles *is a general phenomenon*." Decl. of Peter Gresshoff 2 (Sept. 2, 1992) ('179 Patent) (A56) (emphasis added). The patentee underscored this testimonial throughout the years-long prosecution of the '179 Patent. *See* Resp. to Office Action of May 17, 1994, at 3 (Aug. 30, 1995) ('179 Patent) (A122).

patents cover such correlations regardless of where in the human genome they may be found—or even in the genomes of other animal and plant species. *See* SAC ¶¶ 43-46, 50-71.

Because the alleged discovery set forth in the '179 and '762 Patents is a "law of nature," that alleged discovery is ineligible for patent protection, however "[g]roundbreaking, innovative, or even brilliant" it may have been. *See AMP II*, 133 S. Ct. at 2117; *Mayo*, 132 S. Ct. at 1293.

B. The Additional Steps of the '179 Patent Do Not Make It Patentable Subject Matter.

The SAC references only one claim of the '179 Patent. This claim covers a law of nature and adds additional conventional everyday steps to the process of discovering this law of nature.

Claim 1 of the '179 Patent (*see* SAC ¶¶ 26, 27, 39) recites:

> 1. A method for detection of at least one coding region allele of a multi-allelic genetic locus comprising:
>
> a) amplifying genomic DNA with a primer pair that spans a non-coding region sequence, said primer pair defining a DNA sequence which is in genetic linkage with said genetic locus and contains a sufficient number of noncoding region sequence nucleotides to produce an amplified DNA sequence characteristic of said allele; and
>
> b) analyzing the amplified DNA sequence to detect the allele.

'179 Patent, 59:56-67 (A32). This claim consists of three main parts: a "said primer pair" limitation, an "amplifying" limitation, and an "analyzing" limitation.[10]

The "said primer pair" limitation is the part of claim 1 that "tell[s] the relevant audience about the law[] [of nature] while trusting them to use [that] law[] appropriately." *See Mayo*, 132 S. Ct. at 1297. The limitation informs the audience that the method recited in the claim cannot

[10] As the patentee emphasized to the examiner during prosecution, "*Applicant has not invented a new way to analyze genetic loci*. Rather Applicant has found that when prior art techniques are applied to the non-coding sequences, the result can be more information than analysis of the coding regions." Suppl. Preliminary Am. 6 (Jan. 14, 1993) ('179 Patent) (A66) (emphasis added).

be used unless someone has previously determined "the existence of the gene," "the fact that it is polymorphic," "the sequence of the non-coding genomic DNA region," and "the fact that a non-coding polymorphism [within the non-coding region] is serving as a surrogate marker for a desired physical characteristic, which is created by coding region DNA." *See* SAC ¶ 18. The limitation therefore sets forth the conditions that are "inherently require[d]" in order to "implement[] the [natural law] in the context of the claimed invention," and does not impart any "'inventive concept'" to the claim. *See Ultramercial*, 722 F.3d at 1348.

The "amplifying" limitation "add[s] nothing specific to the law[] of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field." *See Mayo*, 132 S. Ct. at 1299. The specification acknowledges that amplifying DNA using pairs of primers was a well-recognized technique at the time of the alleged invention. '179 Patent, 2:45-60, 3:5-8, 3:39-45, 5:66-6:3, 12:53-65 (A3, A4, A5, A8); SAC ¶¶ 15, 23-25. GTG also states in the SAC that "amplification was known" at the time of the invention. SAC ¶ 25.[11]

GTG's allegation that "no one had used a primer pair to amplify non-coding DNA to define a DNA sequence in genetic linkage with a coding region allele in order to detect that allele," SAC ¶ 25, adds nothing. The only "inventive concept" in the application of conventional amplification techniques to an allegedly new location in nature is attributable solely to the alleged discovery of the law of nature that drove the selection of that location. *See AMP II*, 133 S. Ct. at 2116-17 ("The location and order of the nucleotides existed in nature before Myriad found them. … Myriad's principal contribution was uncovering the precise location and genetic

[11] *See also* Am. in Resp. to Office Action of Jan. 13, 1994, at 11 (July 13, 1994) ('179 Patent) (A109) (describing "methods of selecting primers to amplify a selected region of DNA" as "well known and … within the level of skill in the art"); Resp. to Office Action of May 17, 1994, at 7-8 (Aug. 30, 1995) ('179 Patent) (A126-27) (describing amplification as a "technique[] that w[as] readily practiced by those in skill [sic] at the time the application was filed").

sequence … but separating that gene from its surrounding genetic material is not an act of invention.").

The District Court for the Northern District of California recently held a similar claim invalid under § 101 in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, No. C 11-06391 SI, 2013 WL 5863022 (N.D. Cal. Oct. 30, 2013). In *Ariosa*, the claimed invention involved the application of conventional amplification techniques to a newly discovered target, "paternally inherited cffDNA in [the] maternal plasma or serum" of a pregnant woman. *See id.* at *7. The court held that "the only inventive part of the patent is that the conventional techniques of DNA detection known at the time of the invention are applied to paternally inherited cffDNA as opposed to other types of DNA. Thus, the only inventive concept contained in the patent is the discovery of cffDNA, which is not patentable." *Id.* at *9. Likewise here, the only inventive concept in selecting what to amplify is the alleged discovery of the correlation between polymorphisms in coding and noncoding DNA, which is not patentable.[12]

The final step of claim 1, "analyzing" the amplified DNA, is both "conventional" and "inherently require[d]" in order to use the law of nature. *Ultramercial*, 722 F.3d at 1348; *see* '179 Patent, 16:10-29 (A10).

In sum, claim 1 of the '179 Patent does no more than append to a law of nature limitations that were either "well-understood, routine[, and] conventional" at the relevant time or

[12] GTG also alleges that the DNA strands produced in this "amplifying" step are "synthetic" DNA strands, and "different from the ... naturally occurring DNA from which [they were] produced" in terms of their chemistry and their ability to function within a living organism. SAC ¶¶ 24, 27. Even if these allegations are true, however, the types of (unclaimed) chemical "differen[ces]" that the Complaint describes are irrelevant to the eligibility of the claims, which, as in *AMP II*, "are ... not expressed in terms of chemical composition" and do not "rely in any way on the chemical changes that result from the [amplification] of a particular section of DNA," but rather "understandably focus on the *genetic information* encoded in" the amplified DNA. *See AMP II*, 133 S. Ct. at 2118 (emphasis added).

"inherently require[d]" to "implement[] the [law] in the context of the claimed invention," or both. *See Mayo*, 132 S. Ct. at 1299; *Ultramercial*, 722 F.3d at 1348. In fact, the combination of "well-understood, routine, and conventional" steps specified in claim 1—"amplifying" a DNA sample and then "analyzing" its sequence—was itself "well-understood, routine, and conventional" at the time of the invention. *Ariosa*, 2013 WL 5863022, at *10; *see* '179 Patent, 2:46-55, 3:5-10, 3:45-47 (A3, A4).

The conclusion that claim 1 is drawn to ineligible subject matter is confirmed by the fact that the claim, as asserted by GTG in this suit and in other similar lawsuits, broadly "t[ies] up the future use of [the underlying natural] law[]" and "preempt[s] use of [that law] in all fields." *Mayo* 132 S. Ct. at 1301 (quotation marks omitted); *see* SAC ¶¶ 43-46. The '179 Patent purports to assert ownership over the use of the underlying law of nature in applications including "identifying individuals at risk for or carriers of genetic diseases, … organ transplantation, forensics, disputed paternity[,] and a variety of other purposes in humans," as well as "genetic[] engineer[ing]" of "commercially important plants and animals." '179 Patent, 1:43-49 (A3). GTG has asserted its patents aggressively against businesses engaged in each of these fields. *See* Complaint ¶¶ 29-130, *Genetic Techs. Ltd. v. Agilent Techs., Inc.*, Civil Action No. 11-cv-01389-WJM-KLM (D. Colo. May 25, 2011), E.C.F. No. 1; SAC ¶¶ 43-46. While the ineligibility of the subject matter claimed by the '179 Patent is apparent from its face, "[t]he presence here of the basic underlying concern that th[is] patent[] tie[s] up too much future use of laws of nature simply reinforces [the] conclusion that the processes described in the patent[] are not patent eligible." *Mayo* 132 S. Ct. at 1302.

C. Similarly, the Additional Steps of the '762 Patent Do Not Make It Patentable Subject Matter.

Whereas the '179 Patent purports to claim the use of genetic correlations to determine whether an individual has a certain genetic trait at a particular genetic location, *see* '179 Patent, 3:58-4:20 (A4), the '762 Patent seeks to cover the related, and complementary, process of determining which genetic location is associated with a given trait. '762 Patent, 1:37-41 (A35); *see also id.* 37:41-43, 39:31-32 (A53, A54).

Claim 1 of the '762 Patent, the only claim discussed in the SAC (*see* SAC ¶¶ 27, 42), recites:

> 1. A genomic mapping method for identifying informative, polymorphic markers and using said markers to identify a chromosomal region associated with a trait, comprising:
>
> (a) obtaining a first set of genomic DNA samples from a plurality of individuals representing the diversity of a general population;
>
> (b) amplifying a non-coding sequence from a selected chromosomal region in each of said first set of genomic DNA samples to produce a first set of amplified DNA sequences;
>
> (c) analyzing said first set of amplified DNA sequences to determine whether said non-coding sequence comprises a plurality of polymorphic regions, wherein said plurality of polymorphic regions defines a plurality of haplotypic patterns detectable by a selected technique for analyzing genetic variation;
>
> (d) determining the number of haplotypic patterns associated with said non-coding sequence that are distinct as measured by said selected technique, wherein each haplotypic pattern is a marker for a haplotype of said selected chromosomal region;
>
> (e) repeating steps (a)-(d) to identify a plurality of noncoding sequences, each having a plurality of associated haplotypic patterns, at a series of selected chromosomal regions;
>
> (f) obtaining a second set of genomic DNA samples from a plurality of individuals with the trait from said general population, wherein said plurality of individuals with the trait is not derived from a single family;

> (g) amplifying said plurality of non-coding sequences from said series of selected chromosomal regions in each genomic DNA sample in said second set to produce a second set of amplified DNA sequences;
>
> (h) detecting the haplotypic pattern for each amplified DNA sequence in said second set to identify the haplotype of each corresponding selected chromosomal region;
>
> (i) determining the degree of restriction in haplotype heterogeneity at each selected chromosomal region for said second set of amplified DNA sequences by comparing the number of haplotypic patterns identified for each selected chromosomal region for said first set of amplified DNA sequences and said second set of amplified DNA sequences; and
>
> (j) comparing the degree of haplotype heterogeneity restriction across said selected chromosomal regions, to identify a subseries of adjacent selected chromosomal regions having a greater degree of haplotype heterogeneity restriction at a central selected chromosomal region in said subseries than at selected chromosomal regions at the ends of said subseries as an indication that said central selected chromosomal region is associated with the trait.

'762 Patent, 37:41-38:67 (A53).

Like the steps of claim 1 of the '179 Patent, each of these steps is "well-understood, routine [and] conventional," "inherently require[d]" to "implement[] the [law] in the context of the claimed invention," an "abstract mental process[]," or some combination of the above. *See Mayo*, 132 S. Ct. at 1299; *Ultramercial*, 722 F.3d at 1348; *AMP I*, 689 F.3d at 1334. Steps (a) and (f) require "obtaining a … set of genomic DNA samples from a plurality of individuals." *Id.* 37:45-47, 38:40-44(A53). Obtaining a sample of natural DNA from one or more individuals is not only "well-understood, routine, conventional," but also "inherently require[d]" in a process whose aim is to shed light on the genetic makeup of an individual or a population. *Mayo*, 132 S. Ct. at 1299; *Ultramercial*, 722 F.3d at 1348; *see* '762 Patent, 22:55-58 (A45). Moreover, the Federal Circuit has made clear that when a claim is drawn to a process of analyzing information, a physical sample-gathering step included as a prelude to the analysis cannot confer

subject-matter eligibility on an otherwise ineligible claim. *See In re Grams*, 888 F.2d 835, 840 (Fed. Cir. 1989); *PerkinElmer*, 496 F. App'x at 72.

Steps (b) and (g) involve "amplifying" one or more "non-coding sequence[s]." '762 Patent, 37:48-51, 38:45-48 (A53). As the SAC recognizes, and as is acknowledged in the '762 Patent, this amplification step was "well-understood, routine, [and] conventional" at the time of the alleged invention. *Mayo*, 132 S. Ct. at 1299; *see* '762 Patent, 22:25-42 (A45) SAC ¶ 25. Applying well-known amplification techniques to noncoding sequences, specifically, was not only well known and conventional in itself at the relevant time period, but was also "inherently require[d]" in order to "implement[] the [natural law] in the context of the claimed invention." *Ultramercial*, 722 F.3d at 1348; *see* '762 Patent, 6:23-32 (A37) (describing a prior art reference that discloses "amplification of a … region of exon 12 *and flanking intervening sequences*" (emphasis added)).

Steps (c) and (h) require, respectively, "analyzing said first set of amplified DNA sequences" and "detecting the haplotypic pattern for each amplified DNA sequence." '762 Patent, 37:52-57, 38:49-52 (A53).[13] Once again, these steps were both "conventional" and "inherently require[d]" as of the relevant time period. *Mayo*, 132 S. Ct. at 1299; *Ultramercial*, 722 F.3d at 1348; *see* '762 Patent, 17:49-18:31, 25:11-28 (A43, A47). [14]

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[13] A "haplotype" is a set of polymorphic sites that are inherited together, creating patterns of jointly occurring genetic variations. *See* '762 Patent, 8:30-48 (A38); SAC ¶¶ 11-12, 17, 20.

[14] The prosecution history confirms that at the time of the claimed invention, "[t]echniques for [both] amplifying and analyzing DNA sequences [we]re well known and the application of these techniques to the claimed methods [wa]s well within the level of skill in the art." *See* Am. in Resp. to Office Action of Sept. 21, 1993, at 11 (Dec. 27, 1993) ('762 Patent) (A143); *see also* Am. in Resp. to Final Office Action of March 21, 1994, at 10-11 (June 20, 1994) ('762 Patent) (A162-63) (discussing "the high level of skill in the art" regarding amplification and analysis); *id.* at 13-15 (A165-67) (discussing "[t]he wide applicability of the preferred amplification method, polymerase chain reaction").

Steps (d), (i), and (j) require, respectively, "determining the number of haplotypic patterns," "determining the degree of restriction in haplotype heterogeneity," and "comparing the degree of haplotype heterogeneity restriction." '762 Patent, 38:59-63, 39:52-67 (A53, A54). These are the types of "mental steps" that cannot confer eligibility on a method claim. *See AMP I*, 689 F.3d at 1309, 1334-35. The requirement that "each haplotypic pattern" detected in step (d) be "a marker for a haplotype of said selected chromosomal region" is nothing more than a statement of the natural law: that patterns, or haplotypes, of noncoding-region variation can serve as "markers" for patterns, or haplotypes, of the broader "chromosomal region."

Finally, claim (e) merely instructs the practitioner to "repeat[] steps (a)-(d)." '762 Patent, 38:64-67 (A53).

In sum, each of the steps of claim 1 was "well-understood, routine [and] conventional" as of the time of the claimed invention; "inherently require[d]" to "implement[] the [law] in the context of the claimed invention"; an "abstract mental process[]"; or some combination of the above. *See Mayo*, 132 S. Ct. at 1299; *Ultramercial*, 722 F.3d at 1348; *AMP I*, 689 F.3d at 1334. None of these steps "add[s] *enough* to [the claim's] statement[] of the [natural] correlations" to confer eligibility on the claim. *Mayo*, 132 S. Ct. at 1297. Nor is there anything about the particular combination of steps recited in the '762 Patent that lends "inventiveness" to the claims beyond what the law of nature supplies. Rather, the particular combination of "well-understood, routine, and conventional" steps specified by the claims—sampling a population, amplifying a DNA sequence, analyzing the amplified sequence, and examining the resulting data—was itself "well-understood, routine, and conventional" at the time of the invention. *Ariosa*, 2013 WL 5863022, at *10; *see, e.g.*, '762 Patent, 6:23-32 (A37). In essence, the '762 Patent "simply tell[s practitioners] to gather data from which they may draw an inference," *Mayo*, 132 S. Ct. at 1298,

and does not include any "requirement that a [practitioner] act on" the data in any particular way, *PerkinElmer*, 496 F. App'x at 71. For all these reasons the '762 Patent, like the '179 Patent, claims ineligible subject matter and is invalid.

CONCLUSION

The patents asserted by GTG against BMS do no more than recite a law of nature together with various conventional, necessary, and abstract steps that do not add up to an "inventive concept." *See Mayo*, 132 S. Ct. at 1294. Because "the *only* plausible reading of the patent[s]" is that the claims are not drawn to eligible subject matter, *Ultramercial*, 722 F.3d at 1339, the patents are invalid, and this Court should dismiss GTG's Second Amended Complaint with prejudice for failure to state a claim on which relief can be granted.

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CERTIFICATE OF SERVICE

I hereby certify that on February 3, 2014, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on February 3, 2014, upon the following in the manner indicated:

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